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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,118	03/15/2004	Jui H. Wang	DNPP-02007US0	9185

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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/801,118	WANG ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3-15-04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
The specification to which the oath or declaration is directed has not been adequately identified. See MPEP § 602.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

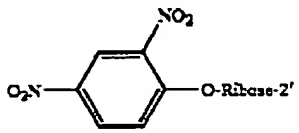
3. Claims 1-4 are rejected under 35 U.S.C. 102(e) as being anticipated by Wang et al. (US 2004/0142896 A1; effective date December 5,2002)

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Wang et al. discloses the following at paragraph [0078]: "[T]he observation that the transition temperature of poly-DNP-RNA/RNA is even higher than that of native RNA/RNA (siRNA) indicates that the DNP-groups not only do not interfere with base-pairing but may aid hybridization via weaker interactions. These observations also suggest that during the derivatization of RNA by the present procedure, the bases themselves are not modified with DNP."

Paragraph [0030] discloses:

> One or more ribose residues in this sequence are modified at the 2'-O-position with a DNP group as shown below.



The above structure meets the structural limitations of the 2'-O-(2,4-dinitrophenyl) group recited in the instant claims, particularly wherein R^2, R^4, and R^5 are hydrogen (paragraphs 0078 and 0030 anticipate instant claims 1-4).

Claim Rejections - 35 USC § 103

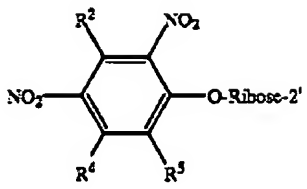
4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-22 are rejected under 35 U.S.C. 103(a) as being obvious over Wang ('438; US Patent No. 6,291,438), and Wang ('988;US Patent No. 5,858,988) in view of Hammond et al. and Parrish et al.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Both Wang ('438) and ('988) describe the use of 2,4-dinitrophenyl groups to modify the 2'-O position of oligoribonucleotides (i.e. short RNA sequences), of between 10 and 40 nucleotides in length (see col. 3, lines 51-67 of '988; and col. 4, lines 6-24):



In another preferred embodiment, R^2, R^4, and R^5 are H. In a preferred embodiment, the oligoribonucleotide has a length of between 10 and 50 nucleotides or alternatively, 10 and 40 nucleotides. In another preferred embodiment, the oligoribonucleotide has a length of between 12 and 30 nucleotides. In another preferred embodiment, the oligoribonucleotide has a length of between 15 and 25 nucleotides.

Moreover, both Wang '438 and '988 (see Summary of the invention in both US Patents) describe the use of 2,4-dinitrophenyl groups for the modification of antisense oligoribonucleotides for the purpose of inhibiting the gene expression, and for use in an antisense therapeutic method.

However, Wang '438 and '988 does not teach the modification of short interfering RNA (siRNA), or the use of siRNA in a therapeutic method.

Hammond et al. teach that antisense and RNA interference are two methods of silencing expression of a gene and that RNA interference possesses characteristics that make it superior to antisense. On page 110, first column, Hammond teaches that antisense methods are straightforward but suffer from "questionable specificity and incomplete efficacy". RNA interference on the other hand, "has been shown in diverse organisms to inhibit gene expression in a sequence-specific manner" (same page and column) and requires only a few molecules of dsRNA per cell to silence expression. Hammond also teaches that the RNA interference phenomenon in animals was discovered by researchers who were using antisense techniques and found that the use

of double stranded instead of single-stranded RNAs reduced gene expression tenfold more efficiently (see paragraph bridging pages 110-111). Hammond et al. do not teach use of siRNAs.

Parrish et al. teach that some common nucleotide modifications, including phosphorothioate, sugar modifications, and terminal cap structures are well tolerated in interfering RNAs.

It would have been obvious to the ordinary skilled artisan at the time of the instant invention to modify the teachings of Wang (both references) to comprise the modification of short interfering RNA (siRNA) with the teachings of Hammond et al. and Parrish et al. One of ordinary skill in the art would have been motivated to make this modification since Hammond et al. clearly teach that RNA interference possesses characteristics that make it superior to antisense. Moreover, one of ordinary skill in the art would have been motivated to make 2,4-DNP modifications of siRNA because the Wang reference clearly teaches that their modifications are suitable for short RNA molecules (i.e. oligoribonucleotides of 10 to 40 nucleotides in length), and Parrish et al. teach that modification of siRNA is feasible and well tolerated in regards to activity.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Omum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

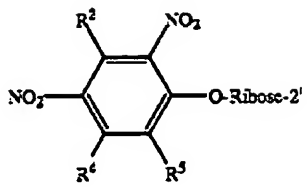
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/284,693. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claim 1 and copending claim 7 are drawn to a short double stranded RNA, wherein at least one nucleotide of one of the complementary strands is modified or derivatized with a 2,4-dinitrophenyl group at the 2'-O position.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 1-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-48 of U.S. Patent No. 6,291,438 or claims 1-63 of US Patent No. 5,858,988 in view of Hammond et al. and Parrish et al.

Both Wang ('438) and ('988) describe the use of 2,4-dinitrophenyl groups to modify the 2'-O position of oligoribonucleotides (i.e. short RNA sequences), of between 10 and 40 nucleotides in length (see claims 1-5 in each patent):



In another preferred embodiment, R^2, R^4, and R^5 are H. In a preferred embodiment, the oligoribonucleotide has a length of between 10 and 50 nucleotides or alternatively, 10 and 40 nucleotides. In another preferred embodiment, the oligoribonucleotide has a length of between 12 and 30 nucleotides. In another preferred embodiment, the oligoribonucleotide has a length of between 15 and 25 nucleotides.

Moreover, both Wang '438 and '988 (see claims in each patent) describe the use of 2,4-dinitrophenyl groups for the modification of antisense oligoribonucleotides for the purpose of inhibiting the gene expression, and for use in an antisense therapeutic method.

However, Wang '438 and '988 does not teach the modification of short interfering RNA (siRNA), or the use of siRNA in a therapeutic method.

Hammond et al. teach that antisense and RNA interference are two methods of silencing expression of a gene and that RNA interference possesses characteristics that make it superior to antisense. On page 110, first column, Hammond teaches that antisense methods are straightforward but suffer from "questionable specificity and incomplete efficacy". RNA interference on the other hand, "has been shown in diverse organisms to inhibit gene expression in a sequence-specific manner" (same page and column) and requires only a few molecules of dsRNA per cell to silence expression. Hammond also teaches that the RNA interference phenomenon in animals was discovered by researchers who were using antisense techniques and found that the use

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9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Janet L. Epps-Ford, Ph.D.
Primary Examiner
Art Unit 1633

JLE

JANET L. EPPS-FORD, PH.D.
PRIMARY EXAMINER